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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/377,081	Applicant(s) GRASSO et al.
	Examiner Christine Saoud	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 19, 2002*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18, 31-34, 39, 43, 44, 46, 47, 49-55, and 57-61* is/are pending in the application.

4a) Of the above, claim(s) *5, 43, 44, 46, 47, 49-55, and 57-60* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6-18, 31-34, 39, and 61* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☒ The proposed drawing correction filed on 19 Feb '02 is: a) ☒ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 45, 48 and 56 have been canceled and claims 4, 6, 12, 18, 31-33 have been amended as requested in the amendment of paper #14, filed 19 February 2002. Claims 1-18, 31-34, 39, 43-44, 46-47, 49-55, 57-61 are pending in the instant application.

Election/Restriction

2. Claims 5, 43-44, 46-47, 49-55, and 57-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Drawings

3. Figure 10 of the instant application is represented by separate panels and/or pages. 37 C.F.R. § 1.84(u)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by **the same number followed by a capital letter**. Applicant is reminded that the Brief Description of the Drawings and the rest of the specification should be amended accordingly to reflect this separate numbering requirement. Applicant did not correct the reference to Figure 10 which should indicate Figures 10A-10B. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3, 7, 8-18, 31-34, and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues that dictionary definitions are provided for homologous, homologue, analog and derivative (exhibits 1-4), and that "these terms, given their ordinary meaning, reasonably convey the full scope of the subject matter of invention to one skilled in the art, and meet all written description requirements". This argument is not persuasive as the terms encompass a genus of molecules for which a complete structure is lacking in the instant specification. Despite the dictionary definitions which Applicant has provided, the instant specification provides definition for the terms used in the claims which must be used when interpreting the claims. The instant claims encompass "homologs, analogs and derivatives" of a purified leptin peptide. The instant specification indicates that these terms are directed to species homologs (page 20), variants which differ from the polypeptide of the present invention "but retaining essential properties thereof" (page 20), peptides which are related to animals, insects, plants, or human leptin (page 21), and that such can be isolated (see page 21) using hybridization techniques. However, the instant specification fails to provide an adequate written description of

such "homologs, analogs or derivatives" such to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is because homologs are usually naturally occurring molecules which have a defined structure which cannot be predicted based on the structure provided in the instant specification. For example, although one of ordinary skill in the art would reasonably expect a given protein to have various allelic forms or have various alternative amino acid substitutions (usually one to three) depending on the source of the protein, one cannot predict what these substitutions will be, therefore, there is not a written description of such. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. In the instant case, as the terms of the claims are defined by function without any recitation of structure, one skilled in the art cannot visualize the identity of subject matter which is claimed. As the instant claims are directed to subject matter which has yet to be described or isolated, the instant specification lacks a written description of this subject matter, absent evidence to the contrary.

6. Claims 1-4, 6-18, 31-34, 39, 45, 48, 56 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a leptin fragment comprising the amino acid sequence of SEQ ID NO:2 or 18 (murine and human, respectively), does not reasonably provide enablement for a leptin peptide lacking these amino acid sequences, such as % homology, amino acid substitutions, derivatives, etc. as recited in the claims. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues that pages 54-58 of the specification discloses "cyclized leptin peptides and D-amino acid substituted leptin peptides, among others". Applicant is correct that the specification discloses that cyclized leptin peptides and D-amino acid substituted leptin peptides could be made, but the specification fails to teach a single leptin peptide which has been altered in this manner and which was tested and found to have modulatory activity on body mass and fails to exemplify a single peptide with a non-naturally occurring amino acid sequence which modulates body mass. As not a single working example exists for leptin peptides modified in this manner, it is uncertain if they will possess modulatory activity on body mass or which substitutions or modifications could be made which would conserve the biological activity of the naturally occurring amino acid sequence.

Applicant argues that percent homology can be determined. However, this argument does not address the rejection of the claimed subject matter in that the instant specification is not enabled for peptides which have % homology (i.e. a certain degree of variation from the naturally occurring amino acid sequences which are enabled).

Applicant argues that *In re Fisher* and Amgen Inc. V. Chugai Pharmaceuticals C. Ltd. are not applicable to the instant application. This argument is not persuasive. The instant specification lacks the appropriate guidance to alter the disclosed peptides (in light of the fact that no alterations have been made) and obtain one with the required activity. The specification is only enabling for leptin peptides having a naturally occurring amino acid sequence (such as SEQ ID

NO:2 or 18) because it does not describe the production of any leptin peptide ***lacking*** that sequence. Applicant's reliance that the specification states that substitutions and derivitizations could be made is not the same as providing examples of molecules which have been altered and found to retain the required biological activity. The specification fails to describe those molecules, other than the peptides of SEQ ID NO:2 and 18, which have body mass modulating ability. Additionally, the pending claims encompass non-naturally occurring mutants of leptin having the disclosed amino acid sequences but does not explicitly identify those amino acid residues which are critical for the biological activity of modulating body mass. In the absence of guidance, a practitioner of the art of molecular biology would have to resort to a substantial amount of experimental trial and error in the form of deletional and substitutional analysis to identify those critical residues as would be needed to produce a mutant of the disclosed peptide. This trial and error would clearly constitute undue experimentation and, therefore, the instant specification is not enabling for the production of such mutants, which are clearly claimed. The standard for an enabling disclosure is not one of making and testing and the claims constitute a "wish to know". Therefore, the claims are not enabled for their full breadth as outlined above.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 4, 6, 8-12, 18, 31, 32, 33, 45, 48, 56, 61, xx are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-11 and 45 are unclear and indefinite for reciting "mammalian", "murine", "human", and "synthetic" in that it is not clear these peptides are to be distinguished one from another when the only physical limitations present are amino acid sequence. In other words, what would make a peptide "human" rather than "synthetic" if they both have the same amino acid sequence? Wouldn't a synthetic peptide which has a human amino acid sequence be a human peptide? Or if a peptide which has an amino acid sequence which is common to both the murine and human peptides, it is human or murine? Applicant may wish to clarify these claims as product by process claims, since the recitation of "mammalian", "murine", "human", and "synthetic" fail to convey any distinguishing limitations for the reasons provided above.

Claim 12 is indefinite for reciting "mouse amino acids" and "human amino acids". Amino acids are neither "mouse" nor "human". It is not clear what is intended by such a recitation as the art fails to distinguish an amino acid from a specific species of animal.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 1-4, 6-18, 39, 45, and 61 are rejected under 35 U.S.C. 102(a/b) as being anticipated by Grasso et al. (Endocrinol. 138:1413-1418, 1997).

Applicant argues that the peptides of Grasso are twice the length of the elected species (SEQ ID NO:18) of the instant claims. This argument is not persuasive as the claims use "comprising" language which is open language and could encompass more than just the amino acid sequence of SEQ ID NO:18. Applicant further argues that Grasso does not provide the leptin polypeptide of SEQ ID NO:18. This argument is not persuasive because the instant claims encompass variants and homologs and derivatives and analogs, which appear to encompass those peptides of Grasso, absent evidence to the contrary.

11. Claims 1, 2, 3, 9, 10, 11, 12, 13, 14, 16, 18, 33, 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Samson et al. (Endocrinol. 137(11): 5182-5185, 1996).

Samson et al. teach a leptin peptide of 35 amino acids which modulates body mass, thereby, anticipating the instant claims. Applicant again argues that the peptide of SEQ ID NO:18 is 7 amino acids in length, however, as the claims recite homology to SEQ ID NO:18, there is no limitation on the length of the peptide. Further, the recitation of analog, homolog and derivative appears to encompass molecules of any size or length, absent evidence to the contrary.

12. Claims 1-4, 6-18, 39, 61 are rejected under 35 U.S.C. 102(a) as being anticipated by Al-Barazanji et al. (WO 97/46585, 12/11/1997).

Al-Barazanji et al. teach leptin peptides, including a peptide which comprises the amino acid sequence of SEQ ID NO:18 (see page 1, lines 35-39), wherein the peptides modulate body

mass, thereby, anticipating the instant claims. Applicant asserts that Al-Barazanji "fails to described any leptin fragments claimed in the invention". This assertion is incorrect. The ob116-149 fragment meets the limitations of the claims.

Allowable Subject Matter

13. Applicant should note that the references cited above fail to specifically teach the 7 amino acid fragment of SEQ ID NO:18. Therefore, a claim limited to a peptide consisting of the amino acid sequence of SEQ ID NO:18 would avoid the prior art of record, as well as meeting the requirements of enablement and written description.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The

examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud